Remarks

Claims 1, 10-12 and 21-26 are pending in the application. Claims 2-5, 9 and 14-20 have been withdrawn from consideration as being drawn to non-elected inventions. Applicant expressly reserves the right to pursue the non-elected inventions in a continuing divisional application. Claims 6-8 and 13-20 have been canceled without prejudice, rendering the claim objections to claims 6 and 7 moot. New claims 21-26 have been added. Applicant addresses the Examiner's rejections, and respectfully requests allowance of the claims in view of the following amendments and remarks.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 7 and 13 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claim 13 has been canceled without prejudice, rendering this rejection moot. The rejections for reciting acronyms "TRAIL" and "JIK" in claims 1 and 7, and for reciting "a biological activity of a polypeptide modulator" in claim 1 are moot in view of the amended claims.

The Office rejected claim 1 as allegedly being indefinite "for the recitation of 'fragment' as it is unclear what portion of the JIK protein is contemplated." (Office Action, page 3). Applicant respectfully disagrees. The amino acid sequence encoding JIK is well-characterized; thus, a "JIK fragment" is clear and definite. Applicant therefore respectfully requests that this rejection be withdrawn.

The Office also rejected claim 1 as allegedly being indefinite "for the recitation 'modulate TRAIL-induced apoptosis' as it is unclear how this step would be performed." (Office Action, page 3). As amended, claim 1 defines that an agent identified in step (a) to modulate JIK kinase activity is further tested in the presence or absence of TRAIL for its ability to modulate TRAIL-induced apoptosis. Accordingly, claim 1 as amended clearly defines how an agent that modulates JIK kinase activity is tested for its ability to modulate TRAIL-induced apoptosis, and Applicant respectfully requests that these rejections be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1, 6-8 and 10-13 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly being nonenabled. Claims 6-8 and 13 have been canceled, rendering the rejection moot as to these claims. Applicant submits that the Office has mischaracterized the claimed invention, and that the claims are enabled.

As described in the specification, the claimed methods are predicated on the discovery of a number of genes that modulate TRAIL-induced apoptosis. Using si-RNA based loss of function screening, the inventors discovered a number of genes that impact TRAIL-induced apoptosis. (See, specification at paragraph 14 and Examples). In the claimed invention, JIK is employed as a novel target for screening modulators of TRAIL-induced apoptosis.

In particular, in step (a) of the claimed method, test agents are first assayed for their ability to modulate the kinase activity of JIK, using routine assays (e.g., as described in the specification at paragraphs 44-56). In step (b), test agents identified in step (a) to modulate the kinase activity of JIK are further tested to confirm their ability to modulate TRAIL-induced apoptosis, using routine assays (e.g., as described in the specification at paragraphs 57-61). The test agents may be applied to cells to be tested for apoptosis activity, and the assay is performed in the presence or absence of TRAIL. If TRAIL-dependent apoptosis activity is altered by addition of the agent identified in step (a) to modulate JIK kinase activity, the agent is confirmed as a modulator of TRAIL-induced apoptosis. (See, specification at paragraph 60).

Contrary to the Examiner's assertions, the specification provides more than sufficient basis for the correlation of JIK and TRAIL-induced apoptosis. As described in Example 5 and Figure 2C, transfection of siRNAs against JIK resulted in a significant increase in TRAIL-dependent caspase activation; thus identifying JIK as a gene that inhibits TRAIL-dependent death. The increase in TRAIL-independent caspase activation is distinctly less than the significant increase in TRAIL-dependent caspase activation. (See, Figure 2C, showing the effects on caspase activity in the absence of TRAIL ("-" columns) vs. under 100 ng/mL TRAIL treatment ("+" column)).

Furthermore, Applicant submits that the disclosure in Zhang, Herr I and Herr II is not relevant to the claimed invention. As the Office correctly noted, Applicant need not demonstrate how JIK affects TRAIL-induced apoptosis. (Office Action, page 7).

Based on the above, the specification teaches how to make and use the invention, and the claimed methods are enabled. Applicant therefore requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1 and 6-8 are rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Tassi et al. (J. Biol. Chem. 274:33287-95 (1999)) "as applied to step a) of the method claims." Claims 1 and 6-8 are also rejected under 35 U.S.C. § 102(a), as allegedly being anticipated by De Souza et al. (Blood 99:3432-3438 (2002)), likewise "as applied to step a) of the method claims." Furthermore, claim 1 is rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Weldon et al. (Surgery 132:293-301 (2002)) "as applied to method step b)." Claims 1 and 12 are also rejected under 35 U.S.C. § 102(a), as allegedly being anticipated by Cantarella et al. (Cell Death and Differentiation 10:134-141 (2003)), likewise "as applied to method step b)." Applicant respectfully disagrees.

The law is clear that the reference must teach every element of the claim to anticipate a claim. MPEP § 2131. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987).

As the Office points out, "[i]t is noteworthy that the Examiner was not able to identify any references describing an inherent or implied relationship between JIK and TRAIL-induced apoptosis." (Office Action, page 8). The Office also notes that the Tassi and De Souza references do not teach step b) of the method claims; and that the Weldon and Cantarella references do not teach step a) of the method claims.

More specifically, the Tassi reference discloses human JIK. The De Souza reference discloses the role of Mst 1 (Ste20 like kinases) in mediating eosinophil apoptosis. Both

references are silent regarding TRAIL-induced apoptosis, or the use of JIK as a target for screening modulators of TRAIL-induced apoptosis.

Weldon teaches that the ability of phorbol ester (PMA) to partially suppress TRAIL-induced cell death was inhibited by BMK1/DN. Cantarella teaches that TRAIL contributes to amyloid-induced neurotoxicity in human SH-SY5Y neuronal cell line. Both references are silent regarding JIK, let alone the use of JIK as a target for screening modulators of TRAIL-induced apoptosis.

Because none of the cited references teaches each and every element of the invention, the invention as claimed is not anticipated. Applicant therefore, respectfully requests that these rejections be withdrawn.

New claims 21-26

New claims 21-26 depend upon claim 1. As previously indicated, none of the references cited by the Office teaches each and every element of the claimed invention. Accordingly, new dependent claims 21-26 which contain all the limitations of claim 1, are not anticipated.

Conclusion

In summary, the claims have been amended to obviate the rejections, and Applicant requests that claims 1, 10-12 and 21-26 be passed to issue. Prior to issuance of a Final Office Action, the undersigned requests a telephonic interview with the Examiner. To expedite prosecution of this application, please telephone the undersigned attorney at 858-812-1539.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-1885** referencing docket No. P1111US10.

Respectfully submitted,

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